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Research Article

Profile and antibiotic susceptibility of urinary pathogenic bacteria in children attending Raparen Hospital, Erbil, Iraq

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Abstract
A urinary tract infection is a colonization of uropathogens anywhere in the urinary tract: kidney, ureter, bladder, and urethra. Most paediatric Urinary tract infections (UTIs) are caused by Gram-negative coliform bacteria arising from faecal flora colonising the perineum, which enter and ascend the urinary tract.The aim of this study was to determine the incidence of UTI among febrile children of different ages presented with specific or non-specific symptoms suggestive of UTI. The samples acquired from children were cultured on MacConkey agar and Blood agar by using disposable loops. The cultures were incubated for 24 hours at 37 °C. The positive cultures were recognized by the bacterial colony features. Gram staining technique was used to distinguish Gram-positive and Gram-negative bacteria, while VITEK® 2 microbial ID/AST was conducted for the entire diagnosis. The study observed the respondents (48.5%) of the participants were 5 – 10 years old, more than one quarter (28.5%) of them were <5 years, the majority (83.8%) were female, and 16.2% of them were male. Regarding culture and sensitivity tests, 46.2% of children had bacteriuria. About 43.8% of infections were caused by Gram-negative bacteria, while only 2.3% were caused by Gram-positive bacteria. *Escherichia coli* was the most common cause of urinary tract infection (UTI), accounting for 32.3%, followed by *Pseudomonas aeruginosa* (3.1%) and only 1.5% of patients had *Staphylococcus Aureus.* The uropathogens were mostly resistant to the cephalosporin group. *E. coli* remained the most predominant uropathogen in children. The results showed that meropenem, imipenem, amikacin, and ciprofloxacin were drug of choice in UTI therapy.

Keywords: Antibiotics, Bacteria, Children infection, Urinary pathogenic bacteria, UTI

INTRODUCTION

Urinary tract infection (UTI) is one of the regular infections in children with a percentage of 1% in boys and 1 –3% in girls, especially in the 1st year of life. In contrast, it starts at 5 years old in girls, and the greatest will be during babyhood and toilet training (Hameed *et al*., 2022). Naturally, bacteria that get to the urinary tract immediately get rid of before they cause any harm by the body's defenses. Nevertheless, occasionally bacteria succeed in causing infection. Cystitis is the name of the bladder infection; urethritis is the name of urethral infection; when the bacteria succeed in travelling up to cause infection in the kidneys it called pyelonephritis (Burd and Kehl, 2011). Urinary tract infection is an infection that includes a variety of clinical manifestations. The most regular bacterial infections in childhood are UTI. Among fevered infants, and sick children with urinary symptoms, 6%–8% will have a UTI (Kaufman *et al*., 2019). The increasing incidence in the first 6 years of life is 2% in boys and 7% in girls (Edlin *et al*., 2013). UTI is responsible for a huge proportion of antibiotic consumption and has a big socio-economic effect (Al-Mijalli, 2017), affecting up to 2.8% of children annually, with recurrence rates ranging from 8% to 30%. It is evaluated that 3.6% of men and 11.3% of women will start one occurrence of urinary tract infection during the children's initial 16 years of lifetime.

Urinary tract infection currency has two style representations, with an initial one within the first 12 months of a lifetime and the later one between 2 and 4 years of it. Following the potty training in the early 6 months of a lifetime, the possibility of UTI is more for men, especially for uncircumcised males. The men to women rates are altered following the first 12 months of a lifetime, with more risk for females that continues into adulthood (Autore *et al*., 2022). Diagnosis in a newborn could be difficult, yet, in older children often present symptoms that mainly go along with urinary tract infection; for example urgency, frequency, dysuria also could show

suprapubic tenderness during examination, from childhood UTI is a supreme factor influencing grown-up health. Children should be medicated at once with suitable antibiotics. Most pediatric UTIs are caused by Gram-negative coliform bacteria that launch into and climb up the urinary tract because of the fecal flora occupying the perineum (Kaufman *et al*., 2019). The most prevalent uropathogen, *Escherichia coli*, is in charge of 80% of pediatric UTIs. To get past host defenses, *E. coli* strains have certain traits, like the ability to adhere fimbriae to the surface of uroepithelial cells. *Klebsiella, Proteus, Enterobacter*, and *Enterococcus* species are some more typical uropathogens (Kaufman *et al*., 2019 ; Al-Mijalli, 2017). The resistance of Gram-negative bacteria to Antimicrobials, especially the Enterobacteriaceae family, has become an important cause of morbidity and chronic medical conditions in public health worldwide (Alatoom *et al*., 2017). Antimicrobial remedy is often given previously to urine culture outcome is available (Belete *et al*., 2019). This study aimed to assess the profile and antibiotic sensitivity pattern of the bacteria causing UTIs in children attending Raparen Hospital, Erbil, Iraq.

MATERIALS AND METHODS

Study area and duration

The study was conducted between July 2022 and October 2022 at Raparen Teaching Hospital for Children in Erbil, Iraq. Urine samples were collected from 161 children and adolescents between the ages of 1 month and 18 years (Alemu *et al*., 2012). The hospital included inpatients, outpatients, and emergency room patients. The data were collected nevertheless of any inclusion or exclusion measurements. All the isolation and antimicrobial sensitivity testing techniques for children were conducted at Raparen Teaching Hospital.

Collection of data

After getting agreement from children's parents, socio-economic and clinical data were collected from patient information collected by nurses. Clean mid-stream urine samples of about 10–20 mL were obtained from patients in wide-mouthed sterile bottles, which were given to their parents for collection and transported to the laboratory immediately after instructing the parents of signed up children to wash their genital area with water and soap to prevent contamination (Derese *et al*., 2016).

Bacterial culture and identification procedure

The samples acquired from children were cultured on MacConkey agar and Blood agar by using disposable loops. Urine cultures were incubated for 24hours at 37 ° C. A positive result of urine was confirmed by a colony count of 10^5 CFU/mL for a midstream urine sample. The positive cultures were recognized by the bacterial colony features. The Gram staining technique was conducted to distinguish Gram-positive and Gram-negative bacteria. The VITEK® 2 microbial ID/AST testing system provided the confidence of fast, accurate results through its design of biochemical reactions and the identification methods using standard microbiological techniques. Its smart design helped ensure better laboratory workflow with fewer repetitive tasks, higher safety, improved standardization, and rapid time-to-results and reporting (Assafi *et al*., 2015).

Antimicrobial susceptibility testing

Antibiotic susceptibility tests were done using the same machine used for identification and final confirmation of the microbe, which is the VITEK 2. The samples were according to the instruction of the machine. The sample needed two tubes, each containing 3 mL of standard solution. The culture was obtained by taking a loop of the bacterial sample from the colony and transmitting it to a test tube with 3 mL of standard solution, where it was mixed until the outcome was a homogenous suspension. The adjustment of turbidity to the density of a McFarland 0.5 to adjust the size of the inoculum (>0.5 and <1.5). If the bacteria were gram-positive, a calibrated micropipette (280 µL) was used. If the bacteria were gram-negative, a calibrated micropipette (145 µL) was used to withdraw the solution from the bacteria-containing tube to the second tube (lesser bacterial density). After placing the ID (identification of the bacteria) kit in the first tube and the AST (antibiotic sensitivity test) kit in the second, the results were received after 6-8 hours. Manually, identification and antibiotic susceptibility tests were done by preparing a suspension by mixing a loopful of bacterial colonies in a tube with 5 ml of normal saline. Then, the adjustment of the turbidity to the density of a McFarland 0.5 in to adjust the inoculum size. A sterile cotton swab was dipped into the suspension, and the bacterial swab was then distributed evenly on the surface of the Mueller-Hinton agar. The cultured plates were left to dry at the temperature of the room for a few minutes. Using sterile forceps, antibiotic discs with different concentrations were applied to the Mueller-Hinton agar.

RESULTS

Table 1 and Fig. 1 show the culture and sensitivity test and the overall background of participants. According to the age of respondents, 48.5% of cases were 5 – 10 years old, more than one quarter (28.5%) of them were <5 years, the majority (83.8%) of cases were female, while 16.2% of them were male. Regarding culture and sensitivity test, more than half (53.8%) of them did not have bacteriuria, in contrast, 46.2% had bacteriuria. About 43.8% of infections were caused by Gram-

negative bacteria, while only 2.3% were caused by Gram-positive bacteria. *E. coli* was the most common causes of urinary tract infection (UTI), accounting for 32.3%, followed by *P. aeruginosa* (3.1%) and only 1.5% of patients had *S*. *aureus* .

The results of the culture and sensitivity test indicated that the majority 90% of the microbial agents or bacteria were sensitive to meropenem, which shown 78.3% sensitive to imipenem and amikacin followed by 68.3% were sensitive to ciprofloxacin, while bacteria had an intermediate reaction to each of ampicillin sulbactam, nitrofurantoin and amoxicillin-clavulanic acid, followed by 5% for each of ceftazidime and gentamycin, 3.3% of cases had an intermediate response to meropenem and amikacin. The bacteria were mostly resistant to ceftazidime (40% of cases), followed by third (33.3%) to cefepime and finally, 26.7% of them had a resistant response for each of ceftriaxone and cefuroxime (Table 2).

Table 3 indicates a non-significant statistical association between culture and sensitivity test and age groups including < 5 years, 5 – 10 years and >10 years. Bacteriuria was present in 50% or less of all age groups. Chi square test was done and p-value was 0.704. Table 4 shows that there was a non-significant statistical association between culture and sensitivity test and gender. Bacteriuria was found in less than 50% of both male and female cases. Chi square test was done and the p-value was 0.741. Outcome of Table 5 revealed that most bacterial isolates were sensitive to meropenem, imipenem, and amikacin and some of them were found to have an intermediate response to imipenem, ciprofloxacin and gentamicin. At the same time, the least of them were resistant to ciprofloxacin, gentamicin.

DISCUSSION

The most regular bacterial infection in childhood is UTI (Kaufman *et al*., 2019, Stein *et al*., 2015, Khan *et al*.). According to a documented study, the epidemiology of UTIs in children relies on some factors like age, gender, and abnormalities in the genitourinary tract (Hanna-Wakim *et al*., 2015). In the present study and according to the age of respondents, 48.5% of cases were 5-10 years old, more than one quarter (28.5%) of them were <5 years, the majority (83.8%) of cases were female, while 16.2% of them were male, the present result agrees with a study conducted in Saudi Arabia 2018 with a result of 81% female and 19% male (Albalawi *et al*., 2018) and the study in Egypt came with the higher female percentage of 74.5% than the male of 25.5% (Rabeea *et al*., 2015). This overall female predominance could be related to circumcision in males, also supposed to be the result of geographic location and religious affiliation. In addition, the shorter

Table 1. Characteristics of the participants and sensitivity of isolated bacteria

Variables	Categories	Frequency	Percent
Age groups	< 5 years	37	28.5%
	5 – 10 years	63	48.5%
	>10 years	30	23.1%
Gender	Male	21	16.2%
	Female	109	83.8%
Culture and sensitivity test	No bacteriuria	70	53.8%
	Bacteriuria	60	46.2%
Type of bacteria	None	70	53.8%
	Gram negative	57	43.8%
	Gram positive	3	2.3%
Bacterial isolates	None	70	53.8%
	Escherichia coli	42	32.3%
	Pseudomonas aeruginosa	4	3.1%
	Klebsiella pnuemoniae	4	3.1%
	Klebsiella sp.	3	2.3%
	Staphylococcus aureus	2	1.5%
	Morganella morganii	1	0.8%
	Proteus mirabilis	1	0.8%
	Pseudomonas sp.	1	0.8%
	Proteus sp.	1	0.8%
	Staphylococcus sp.	1	0.8%
Total		130	100

Table 2. Percentages of antibiotic sensitivity tests

Antibiotic	Sensitive No. (%)	Intermediate No. (%)	Resistant No. (%)
Pipercillin / tazobactam	12 (20%)	1 (1.7%)	2 (3.3%)
Ceftazidime / avibactam	8 (13.3%)	0 (0%)	0 (0%)
Ceftolozan / etazobactam	8 (13.3%)	0 (0%)	0 (0%)
Imipenem	47 (78.3%)	1 (1.7%)	2 (3.3%)
Meropenem	54 (90%)	2 (3.3%)	3 (5%)
Amikacin	47 (78.3%)	2 (3.3%)	5 (8.3%)
Ciprofloxacin	41 (68.3%)	1 (1.7%)	10 (16.7%)
Ceftazidime	28 (46.7%)	3 (5%)	24 (40%)
Gentamycin	36 (60%)	3 (5%)	12 (20%)
Cefepime	24 (40%)	0 (0%)	20 (33.3%)
Trimethoprim	16 (26.7%)	0 (0%)	10 (16.7%)
Ampicillin sulbactam	2 (3.3%)	4 (6.7%)	1 (1.7%)
Cefotaxime	7 (11.7%)	1 (1.7%)	12 (20%)
Nitrofurantoin	18 (30%)	4 (6.7%)	6 (10%)
Amoxicillin clavulanic acid	20 (33.3%)	4 (6.7%)	11 (18.3%)
Ceftriaxone	10 (16.7%)	1 (1.7%)	16 (26.7%)
Cefuroxime	7 (%)	1 (1.7%)	16 (26.7%)
Trimethoprim sulfamethoxazole	8 (13.3%)	0 (0%)	18 (30%)

Table 3. Association between bacterial culture and age of the participants

		Bacterial culture		Total
		No bacteriuria	Bacteriuria	
Age groups	< 5 years	22	15	37
		59.5%	40.5%	100%
	5 – 10 years	33	30	63
		52.4%	47.6%	100%
	>10 years	15	15	30
		50%	50%	100%
Total		70	60	130
		53.8%	46.2%	100%

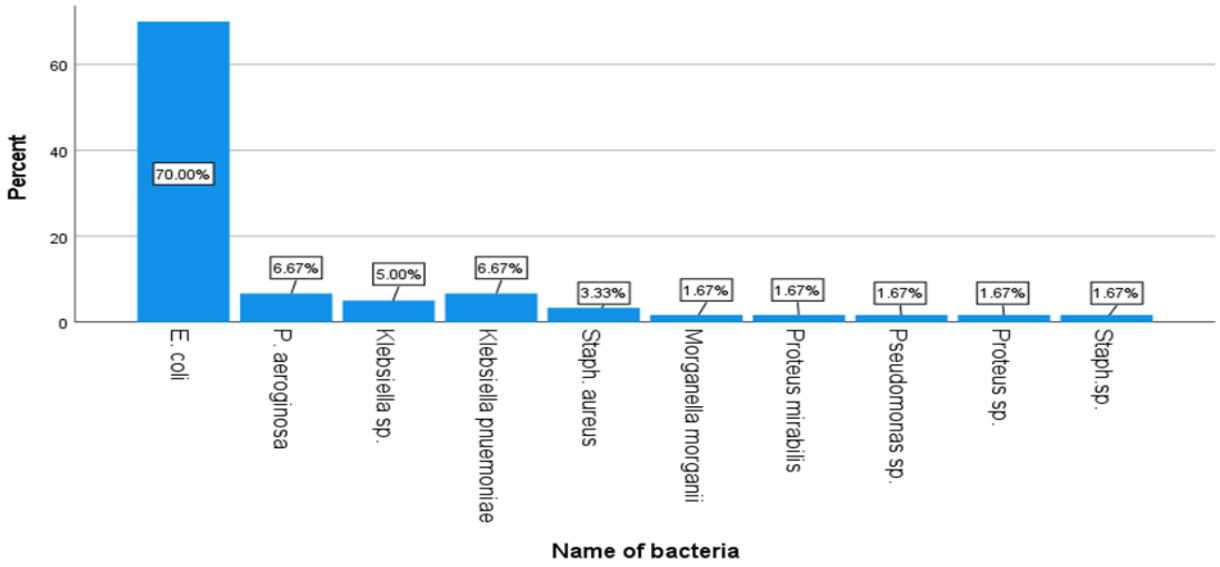

Fig. 1. *Bacterial isolates among affected patients*

Table 4: Association between bacterial culture and gender.

		Culture and sensitivity test		Total
		No bacteriuria	Bacteriuria	
Gender	Male	12	9	21
		57.1%	42.9%	100%
	Female	58	51	109
		53.2%	46.8%	100%
Total		70	60	130
		53.8%	46.2%	100%

Table 5. Difference in antibiotic sensitivity among bacterial isolates.

Isolates	Type	Mero-penem	Imipenem	Amikacin	Ciprofloxacin	Gentamicin	TSX*
E. coli	S	39 (92.9%)	36 (85.7%)	37 (88.1%)	33 (78.6%)	29 (69%)	13 (31%)
	I	1 (2.4%)	0 (0%)	0 (0%)	0 (0%)	1 (2.4%)	0 (0%)
	R	2 (4.8%)	1 (2.4%)	2 (4.8%)	6 (14.3%)	7(16.7%)	7(16.7%)
P. aeruginosa	S	4 (100%)	4 (100%)	3 (75%)	1 (25%)	2 (50%)	0 (0%)
	I	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	R	0 (0%)	0 (0%)	1 (25%)	2 (50%)	2 (50%)	0 (0%)
K. pnuemoniae	S	3 (75%)	4 (100%)	3 (75%)	2 (50%)	3 (75%)	3 (75%)
	I	1 (25%)	0 (0%)	1 (25%)	1 (25%)	1 (25%)	0 (0%)
	R	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)
Klebsiella sp.	S	3 (100%)	2 (66.7%)	1 (33.3%)	3 (100%)	1(33.3%)	0 (0%)
	I	0 (0%)	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	R	0 (0%)	0 (0%)	1 (33.3%)	0 (0%)	1(33.3%)	1 (33.3)

* TSX=Trimethoprim sulfamethoxazole; S=Sensitive; I=Intermediate; R=Resistance

female urethra is a crucial reason (Hanna-Wakim *et al*., 2015).

Regarding culture and sensitivity tests, more than half (53.8%) of them did not have bacteriuria; in contrast 46.2% had bacteriuria. Usually, 43.8% of infections are caused by Gram-negative bacteria, while only 2.3% are caused by Gram-positive bacteria. These results agree with studies conducted in Austria, Italy, Ethiopia and UAE (Khan *et al*., Autore *et al*., 2022, Kaufman *et al*., 2019, Belete *et al*., 2019). The majority of UTIs caused by uropathogens (Gram-negative bacteria) present in the periurethral area and the fecal flora will ascend to the bladder along the urethra and also may reach the kidneys via the ureters, which causes pyelonephritis (Kaufman *et al*., 2019, Albarrak *et al*., 2021). The major mechanisms embrace fimbriae that stimulate adhesion to urothelial cells, flagella-mediated motility and eventually provide resistance to certain antibiotics (Oliveira and Mak, 2020). The data of the present study showed that the majority of the uropathogen were *E. coli* isolates with a percentage of almost 70% of all the other uropathogens. This result agrees with other studies made in Ethiopia, United States of America, India, Iraq and Jordan, with similar percentages of 73.2%, 79%, 66.25%, 65.9% and 72.9%, respectively (Oliveira and Mak, 2020, Edlin *et al*., 2013, Mohamed *et al*., 2022, Sood *et al*., 2015, Alshara, 2011). In this regard and the reason that involve *E. coli* is the most abundant bacteria might be due to having genes that increase host tissue attack and bacterial survival, and the presence of fimbriae assists bacterial attachment to the uroepithelial cell surface to let the bacteria defeat the host defenses and clear the way to the tissue exposure to more virulence factors, such as hemolysin and lipopolysaccharide (LPS), also the toxins produced by *E. coli* could affect the normal functions of the cells or lead to cell death (Kaufman *et al*., 2019, Oliveira and Mak, 2020).

In the present study, less common bacteria were *Pseudomonas aeruginosa, Kleipsiela pneumonia,* with the same percentages of 6.67%. This study agrees with studies conducted in Ethiopia where *Pseudomonas aeruginosa* and *Kleipsiela pneumonia* were also the second and third most abundant two bacteria after *E. coli* with different percentages (Oliveira and Mak, 2020), The present study conducted only one Gram positives bacteria which was *Staphylococcus sp.* with a percentage of 1.67%, this study is not comparable with other studies conducted in other countries with higher percentages of *Staphylococcus* sp., in Ethiopia, USA and Italy (Autore *et al*., 2022, Edlin *et al*., 2013) This

may be because bacterial etiologies vary with different geographical regions even vary over time within a population. Circumcisions in males, periurethral microflora, micturating problems, bowel abnormalities, local factors, and hygienic measures are crucial in UTI pathogenicity (Sawalha, 2009).

The sensitivity test indicated that the majority 90% of the microbial agents were sensitive to meropenem, 78.3% of cases were sensitive to imipenem and amikacin followed by 68.3% of them were sensitive to ciprofloxacin. In this regard the results agree with another study with 100% sensitivity of bacteria for both the carbapenems Imipenem and Meropenem (Sahu *et al*., 2018). Furthermore, in another study conducted, more than 98% of the isolates were sensitive to Imipenem and Mepenem, while 86.36% were sensitive to amikacin with good susceptibility to ciprofloxacin (88.23%) (Biswas *et al*., 2014), also studies showed that the most active drugs were Imipenem and Meropenem (Gales *et al*., 2000, Hossain *et al*., 2020).

This study observed a significant increase of resistance to cephalosporins second, third and fourth generations, which agrees with the other study made in Lebanon. This might be due to the overuse and misuse of antibiotics in the community, specifically third-generation cephalosporins. Considering the increasing resistance, the dependence on the cephalosporins family will increase the need for new alternative antibiotics (Hanna-Wakim *et al*., 2015). The prevalence of pathogens resistant to antibiotic therapy varies widely in different geographical areas (Autore *et al*., 2022).

Conclusion

The present study concluded that *E. coli* remained the most predominant uropathogen in children and antibiotics viz. meropenem, imipenem, amikacin, and ciprofloxacin were the drug of choice in UTI therapy. The resistance of not less than one antibiotic-imipenem, ciprofloxacin and gentamicin that were commonly prescribed was high. Therefore, the guidelines for treating UTI should be reevaluated from time to time based on local studies, and new health guidelines should be encouraged for a safe prescription of antibiotics.

Conflict of interest

The authors declare that they have no conflict of interest.

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